October 23, 1956

Dr. J. Lein
Bristol Laboratories
Syracuse 1, N.Y.

Dear Joe:

I am very pleased to hear of your active interest in the dap-analogue possibilities. I have to say this is going to be a fairly obvious idea, as a number of people are becoming interested in specific constituents of cell walls and it will only be a matter of time before this becomes an apparent therapeutic lead. However, until now I have not heard anyone mention it: possibly for the same reason that I will keep your confidence on the subject.

We have your sample of C329 & will doubtless give it some trial. We are somewhat hesitant to go very deeply into it until it becomes public property. But on the same basis, I will be very glad to look at your other antibiotic for wall effect. In fact, we might be able to exchange a service if you wanted to round up a collection of the other antibiotics on the market (except the most common ones-- we have tried so far only streptomycin, tetracycline, bacitracin & have some chloramphenicol handy) & we would test them in this system.

I don't know why gram-negatives are generally more resistant to penicillin: it may have to do with the penetration of the drug, or intracellular penicillinase, but this is only speculation until the target enzyme is picked out.

The main point I wanted to bring out now was the identification of another unique wall component, which seems to be quite general: an R-3-glucosamine where R is probably $-CH_2-CHOH-COOH$. This is rather an unusual compound, and chemical imitation might be difficult, but on the same lines as the DAP-analogues it would be worthwhile looking at other R substitutions. R= CH_3 would probably be the easiest to set up, but might not be enough alike. But there it is for whatever you want to do with it. The work on this hexosamine is being done by Strange (cf. J.Gen.Microbiol. 15, xii,8/56) at Porton; I heard about the chemical structure from Powell (also at Porton) at a seminar she gave here.

Yours sincerely,

Joshua Lederberg